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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,775	03/08/2005	Yasuo Suda	12480-000105/US	5852
30593 7590 02/09/2007 HARNESSE, DICKEY & PIERCE, P.L.C. P.O. BOX 8910 RESTON, VA 20195			EXAMINER HAQ, SHAFIQL	
			ART UNIT	PAPER NUMBER
			1641	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		02/09/2007	PAPER	

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/526,775	<b>Applicant(s)</b> SUDA ET AL.	
	<b>Examiner</b> Shafiqul Haq	<b>Art Unit</b> 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 17 April 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08 March 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>3/8/05, 6/8/05</u> | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

1. some of the NPL and other documents cited in IDS have not been considered because copies of those documents were not provided. In order to be in compliance with MPEP 609, III, A (2), applicants must provide copies of all of the references cited in the IDS. These references will become part of the official file of this application. Upon receipt of the missing documents, they will be considered by the examiner when preparing the next office action and a signed copy of form PTO-1449 will be provided with the next office action.

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-7, 12-17, 19-22 and 24-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.
4. Claim 1 recites the phrase "multi-branched structure moiety including three or four hydrocarbon derivative chains". It is not clear how the hydrocarbon derivative chain is arranged or branched at "X". The chemical nature and structure of the hydrocarbon derivative chain is also unclear.
5. Claim 4 recites a linker compound according to claim 1 and recites a linker compound represented by formula (3). Thioctic component is a required part of the compound of claim 1 but in formula (3), the thioactic component is missing.

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Therefore, it is confusing whether formula (3) is intended to represent "X" of formula (1) or is a distinct linker compound.

6. With regard to claim 12, the nature and structure of the amine compound reacted with thioctic acid is vague and indefinite. It is also unclear what linker compound is intended to be produced in this method. Is it for producing linker compound of formula 1 or for producing linker compounds not disclosed in any of the proceeding claims?
7. Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: protecting reaction steps, condensation reaction steps and deprotecting reaction steps.
8. Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: reductive amination reaction steps.
9. With respect to claims 14, 15, 19 and 22, the term "supporter" is not a common terminology. Applicants are advised to replace the term with "support".
10. Claims 14, 18 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: reaction steps for introducing sugar molecules.
11. Claims 16, 17, 20, 21, 24 and 25 provide for using the ligand carrier for plasmon resonance measurement and for affinity chromatography, but, since the claims do

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not set forth any positive steps how the use is practiced, it is unclear what method/process steps applicant is intending to encompass for the use of the ligand carrier. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claim 1-5, and 13-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for hydrocarbon derivative chain comprising C-C bond, C-N bond, CO-NH bond and an aromatic amino group, do not reasonably provide enablement for all hydrocarbon derivative chains represented by the bond as defined in the specification (page 5, lines 2-8). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The term "hydrocarbon derivative chains", as defined in specification consists is a hydrocarbon chain, having an aromatic amino group at an end thereof, part of whose C-C bond serving as backbone structure of the hydrocarbon chain, may be replaced with a C-N, a C-O and an amide bond (page 5, lines 2-8). This definition encompasses many backbone structures including poly-ethylene oxide (PEG).

The specification provides guidance and working examples for linker compounds having hydrocarbon derivative chains comprising aromatic amino group at an end,

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and backbone structures comprising C-N bonds and amide bonds for linker compounds but there is no enablement in the specification for use of all other backbone structures (e.g. containing poly-ethylene oxide. PEG). As for example, PEG having an aromatic amino group at the end will not be able to produce a branched structure (e.g. four PEG chains branching out from X) unless there is a nitrogen atom attached to a carbonyl (i.e. amide bond) group of formula (1) of claim 1.

### ***Claim Rejections - 35 USC § 101***

14. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

15. Claims 16, 17, 20, 21, 24 and 25 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

### ***Claim Rejections - 35 USC § 103***

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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17. Claims 1-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hayashi et al (Tentative Lecture Proceeding, Chemical Society of Japan 2001) in view Sumida et al (JP 2002-80488 A) and Tomalia et al (US 5,714,166) and further in view of Nelson et al (US 6,756,345 B2).

Hayashi et al. disclose a linker compound wherein a branched structure containing two hydrocarbon derivative chain having a terminal aromatic amino group is bonded to a biotin terminal (see compound 1). Saccharides (e.g. heparin partial disaccharide structure (G1cNS6S-IdoA2S)) are then linked to amino group attached to benzene ring by reductive amination reaction to prepare compound 2 ligand. Hayashi et al also disclose that by taking advantage of biotin-streptoavidin affinity, compound 2 was arranged on a surface of a sensor chip having streptoavidin immobilized thereon. A surface plasmon resonance measurement method for detecting interaction of saccharides with the ligand is also disclosed.

Hayashi et al disclose two hydrocarbon derivative chain in a branch chain structure. Hayashi et al., however, do not disclose three or four hydrocarbon derivative chains in a branched chain structure as claimed in present application.

Sumida et al disclose a ligand having oligosaccharide/phenylene diamine complex compound. The reference disclose that three to five hydrocarbon derivative chains having saccharides bonded to terminal aromatic amino groups may be provided (see abstract and pages 1-7) and both the references of Hayashi and Sumida share the common feature that they both have same hydrocarbon derivative chain structure, and have a ligand structure capable of collecting oligosaccharide

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chains and a person skilled in the art would easily understand that increasing the hydrocarbon chain having terminal aromatic amino group in the linker compound would enable the collecting of saccharides to be carried out more efficiently.

Tomalia et al in a method of producing targeted dendrimer conjugates disclose that symmetric starburst polymer (e.g. PAMAM) having polybranched arm gives significant advantages which can provide a means for the delivery of high concentrations of carried materials per unit of polymer (column 1, lines 38-42) and disclose that branching can be increased at terminal amino group on a preceeding generation branch (see PAMAN in column 28 and branching strategy in column 30, G=1 and G=2 and G=3 in column 31). Tomalia et al also disclose protecting and deprotecting steps to protect amino groups and deprotect for reaction to occur. Tert-butoxycarbamate is preferred protecting group which can be deprotected by mild acid hydrolysis.

Therefore, given the above fact that increasing the number of derivative chain is advantageous for concentrating and detecting interacting biomolecules (Yomalia et al) and branch chain can be increased at amino terminal group (Yomalia et al), it would have been prima facie obvious to one of ordinary skill in the art at the time of the instant invention to increase the derivative chain of Hayashi et al., from 2 to 4 from the teaching of Sumida et al, with the expectation of producing similarly useful linker compound. The method steps of claim 8 would be obvious considering that protecting and deprotecting steps for amino groups are well known in the art (Tomalia et al) and protection of aromatic amino groups using well known protecting



group (e.g. t- butoxycarbamate) before attaching biotin molecule is inherently present in the reaction step for generating the reference compound of formula 1 (Hayashi et al).

Hayashi et al., Sumida et al and Tomalia et al (US 5,714,166) however, do not disclose using dithiolane anchoring group for attaching the ligand to solid surface such as for attaching to sensor chip surface. However, use of dithiolane for anchoring ligands on solid surface is well known in the art of biosensors.

Nelson et al. disclose a ligand comprising dithiolane group for preparing self-assembled monolayer on metal (e.g. gold) surfaces. The composition provides a highly versatile tethers suitable for immobilization on a metal backbone. Nelson et al. disclose several advantage of using 1,2 dithiolane (i.e. tethering group containing cyclic S-S-) in columns 4-6. One particular advantage is, when bound to metal surface, a 1,2-dithiolane composition of the invention is chemically stable in a wide variety of hostile media and conditions (column 5, lines 1-4). Another advantage cited is that 1,2-dithiolane is thioctic acid, d-thioctic acid (i.e. lipoic acid as disclosed in claim 17 of present application) or derivatives and d-thioctic acid is a natural substance found in mammals and thus are physiologically compatible.

Therefore, given the above fact the 1,2 dithiolane (i.e. tethering group containing cyclic S-S-) is advantageous for its stable association with gold surface and is physiologically compatible, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute biotin anchoring group with cyclic -S-S- group (e.g. 1,2-dithiolane, specially lipoic acid) in the tethering residue

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of Hayashi et al, with the expectation of obtaining sensor chip stably associated with the linker compound with a reasonable expectation of success.

### ***Double Patenting***

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 1-25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-28 of copending Application No. 10/526,938 in view of Nelson et al (US 6,756,345 B2).

Copending application disclose a linker compound which is similar to the linker compounds of instant application differing only by anchoring group that attaches the linker compound to a solid surface. Copending application disclose biotin as anchoring group whereas the anchoring group in the compounds of present application is dithiolane group of thioctic acid.

Nelson et al. disclose a ligand comprising dithiolane group for preparing self-assembled monolayer on metal (e.g. gold) surfaces. The composition provides a highly versatile tethers suitable for immobilization on a metal backbone. Nelson et al. disclose several advantage of using 1,2 dithiolane (i.e. tethering group containing cyclic S-S-) in columns 4-6. One particular advantage is, when bound to metal surface, a 1,2-dithiolane composition of the invention is chemically stable in a wide variety of hostile media and conditions (column 5, lines 1-4). Another advantage cited is that 1,2-dithiolane is thioctic acid, d-thioctic acid (i.e. lipoic acid as disclosed in claim 17 of present application) or derivatives and d-thioctic acid is a natural substance found in mammals and thus are physiologically compatible.

Therefore, given the above fact the 1,2 dithiolane (i.e. tethering group containing cyclic S-S-) is advantageous for its stable association with gold surface and is physiologically compitable, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute biotin anchoring group with cyclic -S-S- group (e.g. 1,2-dithiolane, specially lipoic acid) in the tethering residue in the compounds of copending application, with the expectation of obtaining sensor chip stably associated with the linker compound with a reasonable expectation of success.

This is a provisional obviousness-type double patenting rejection.

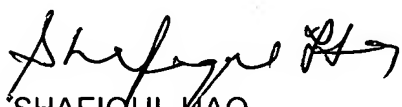
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**Conclusion**

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shafiqul Haq whose telephone number is 571-272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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